INTERNATIONAL SEARCH REPORT

International appli

PCT/US04/36456

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G06F 19/00

US CL : 702/27

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 6; 702/19, 20, 27

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST/WEST, STN, MedLine, Biosis, CAPlus

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 6,269,312 B1 (Mayo et al.) 31 July 2001 (31.07.2001), see especially Abstract, column 1, line 14 through column 2, line 64, and column 5, line 30 through column 30, line55.	1-3, 38 --- 4, 5, 7, 11-17, 19, 21-27, and 32-35
Y	Wang et al. "Fourier Transform Ion Cyclotron Resonance Mass Spectrometric Detection of Small Ca2+-Induced Conformational Changes in the Regulatory Domain of Human Cardiac Troponin C" J Am Soc Mass Spectrom, 1999, Vol. 10, pages 703-710, see escpecially Abstract and pages 703, first column, line 1 through page 708, column 1, line 23.	4, 5, 7, 11-17, 19, 21-27, and 32-35
Y	Wang et al. "A Transition-State Analogue Reduces Protein Dynamics in Hypxanthine-Guanine Phosphoribosynyltransferase", Biochemistry, 2001, 40, 8043-8054, see especially Abstract and page 8043, column 1, line 1 through page 8048, column 2, line 37.	4, 5, 7, 11-17, 19, 21-27, and 32-35
X,E A	US 2004/0153256 A1 (Woods) 05 August 2004 (05.08.2004), see especially Abstract, Figures 1 and 3, and paragraphs 0034-0048, and 0069-0082 Boesen et al. "Crystallization and preliminary crystallographic studies of Human TGF-beta type II receptor ligand-binding domain" Acta. Cryst. (2002) D58, pages 1214-1216	1-37

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 June 2005 (03.06.2005)	27 JUN 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-8300	Authorized officer Eric S. DeJong EDJ Telephone No. (571) 272-6099

J.S. Brusca 5 June 2005

JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER

Form PCT/ISA/210 (second sheet) (January 2004)

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INTERNATIONAL SEARCH REPORT

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C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Weselucha-Birczynska et al. " Flexibility of CuCl-tetrahedra in Bis[Cinchoninium Tetrachlorocuprate(II)]trihydrate Single Crystals. X-Ray Diffraction and EPR studies" Inord. Chem., 2001, 40, pages 4526-4533.	
A	Day et al. "Isolation, Characterization, and preliminary X-ray Diffraction Data for a Serine Protease from Penicillium cyclopium" The Journal of Biological Chemistry, Vol. 261, No. 4, February 5 1986, pages 1957-1961.	

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This International Search Authority has found 2 inventions in the International Application covered by the claims indicated below: This application contains the following inventions or groups of invention which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional fees must be paid.

Group I, claims 1-37, drawn to a method of three-dimensional structure prediction and/or determination of a protein of interest of unknown structure comprising comparing rates of exchange with experimental hydrogen exchange analysis.

Group II, claims 38-44, drawn to a method of three-dimensional structure prediction and/or determination of a protein of interest of unknown structure comprising comparing calculated rates of hydrogen exchange using thermodynamic parameters.

This international Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the reasons indicated below.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The common concept between the inventions of Groups I and II is a method of three-dimensional structure prediction and/or determination comprising comparing calculated amide hydrogen exchange rates and is already well known in the art. See Mayo et al. (P/N US 6,188,965 B1), Abstract and column 33, lines 48-61.Therefore the special technical feature linking the inventions of Groups I and II does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The Special Technical Feature of Group I is considered to be a method of three-dimensional structure prediction and/or determination of a protein of interest of unknown structure, said method comprising comparing calculated rates of amide hydrogen exchange determined for a set of predicted possible structures for said protein of interest with the experimental hydrogen exchange analysis of said protein of interest, and identifying one or more structure from said set of predicted possible structures having a calculated exchange rate profile closely matching the experimental exchange rate profile.

The special Technical Feature of Group II is considered to be a method of structure prediction and/or determination of a protein of interest of unknown structure, said method comprising comparing calculated rates of amide hydrogen exchange determined for a set of predicted possible structures for said protein of interest using thermodynamic parameters of each amino acid residue in said protein of interest defined by hydrogen exchange analysis with experimental hydrogen analysis of said protein, and identifying one or more structures from said set of predicted possible structures having a calculated exchange rate profile closely matching the experimental exchange rate profile.